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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,544	04/27/2001	Defu Zeng	STAN 190	3043

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/844,544	ZENG ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☒ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see below*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *none*.

   Claim(s) objected to: *none*.

   Claim(s) rejected: *1,2,6-8,10,12 and 13*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *See Continuation Sheet*

Marianne DiBrino 4/7/04

Continuation of 3. Applicant's reply has overcome the following rejection(s): the rejection at item #2 under 35 USC 112, first paragraph enablement in the Final Rejection mailed 10/21/03.

Continuation of 10. Other: The rejections of record under 35 USC 103(a) at items 5 and 6 of the Final Rejection mailed 10/21/03 stand for the reasons of record and in addition, the following reasons. Applicant's arguments in Applicant's amendment after final filed 12/19/03 have been fully considered, but are not persuasive. Applicant's arguments are of record in the said amendment and including in the Declaration of Dr. Samuel Strober under 37 CFR 1.132 filed with the said amendment. It is the Examiner's position that the references Hughes and Kotzin are argued separately. It is the Examiner's further position that one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success. As enunciated in the Examiner's rejection at item #5 in the said Final Rejection, Applicant used the NZB/NZW model of lupus, and Amano et al teach "More recent studies have shown that the spontaneous secretion in vitro of both IgM and IgG by spleen cels from lupus-prone New Zealand Black/New Zealand White [i.e., NZB/NZW] mice is mediated by the CD1 high subset of B cells", i.e., that spontaneous antibody secretion in the same disease model used by Applicant is mediated by CD1 positive B cells. In addition, it is the Examiner's further position that in contrast to Applicant's assertion (that of key importance is that the injection of double negative cells which correspond to the cells that originally expressed the transgene, were protective of the disease, while the single positive cells which do not correspond to the original cell type caused a disease phenotype, that one of skill in the art would have reason to believe that the cells tested by Amano et al which expressed a Vb9/Va4.4 TCR, in a double negative cell would prevent disease and in a single positive cell after transfer to a secondary host would be pathological for SLE) one of skill in the art could not conclude with any degree of certainty that CD1 would have a causative effect in spontaneous lupus, Zeng et al teach that SLE inducing cells, i.e., the single positive T cells, secreted large amounts of IFN-g and little IL-4 and the SLE preventive cells, i.e., the double negative cells, secreted large amounts of IL-4 and little IFN-g and little IL-10 (especially page 525 first column and abstract). It is the Examiner's position that Zeng et al further teach that introduction of an IL-4 transgene into NOD or NZW X c57BL/6 mice prevents SLE, that in hereditary murine lupus, administration of IL-10 worsens the disease. "It is not surprising that T cells that secrete high levels of IFN-g and IL-10 and low levels of IL-4 such as the transgenic anti-CD1 CD4+ cells may induce or worsen lupus after activation of their CD1 receptors. One the other hand, the transgenic and low levels of IFN-g and no IL-10 would have been predicted to ameliorate disease based on their cytokine secretion pattern" (especially paragraph spanning columns 1 and 2 on page 534). Zeng et al also teach "The cytokine secretion pattern of the T cells plays a critical role in regulating the B cell activation even when the TCR of the T cell subsets and the CD4 and CD8 receptor expression are identical". "...NZB/NZW F1 mice lose a subset of T cells..that recognizes CD1 and secretes high levels of IL-4 just before lupus develops. Anti-Va14 monoclonal antibodies injected into MRL/lpr mice exacerbates the development of lupus, and depletes this T cell subset...The latter subset shows two characteristics (recognition of CD1 and high level secretion of IL-4) with the CD4-CD8- T cell subset in the marrow that prevented lupus in this study. Zeng et al teach that "the interaction between anti-CD1 T cells and B cell expressing surface CD1 leads to the activation of both cell types that results in hypergammaglobulinemia and systemic autoimmunity in vivo." It is the Examiner's position that one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success from the teachings of the combined references.

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